

CLAIMS

What is claimed is:

1. A method of classifying a lymphoma sample according to predicted treatment outcome comprising the steps of:
 - 5 a) isolating a gene expression product from at least one informative gene from one or more cells in said sample; and
 - b) determining a gene expression profile of at least one informative gene, wherein the gene expression profile is correlated with a treatment outcome, thereby classifying the sample with respect to treatment outcome.
- 10 2. A method according to Claim 1, wherein the lymphoma sample is a diffuse large cell lymphoma sample.
3. A method according to Claim 1, wherein the gene expression product is mRNA.
4. A method according to Claim 3, wherein the gene expression profile is determined using hybridization probes specific to at least one informative gene.
- 15 5. A method according to Claim 3, wherein the gene expression profile is determined using oligonucleotide microarrays.
6. A method according to Claim 1, wherein the gene expression product is a peptide.
7. A method according to Claim 6, wherein the gene expression profile is
20 determined using antibodies.

8. A method according to Claim 1, wherein the predicted treatment outcome is survival after treatment.
9. ~~A method according to Claim 1, wherein the informative gene is selected from the group consisting of the genes in Figure 1.~~
- 5 10. ~~A method according to Claim 1, wherein the informative gene is selected from the group consisting of the genes in Figures 2A and 2B.~~
11. A method of assigning a diffuse large cell lymphoma sample to a treatment outcome class, comprising the steps of:
- 10 a) determining a weighted vote for one of the classes of one or more informative genes in said sample in accordance with a model built with a weighted voting scheme, wherein the magnitude of each vote depends on the expression level of the gene in said sample and on the degree of correlation of the gene's expression with class distinction; and
- 15 b) summing the votes to determine the winning class, wherein the winning class is the treatment outcome class to which the diffuse large cell lymphoma sample is assigned.
12. The method of Claim 11, wherein the weighted voting scheme is:

$$V_g = a_g (x_g - b_g),$$

20 wherein V_g is the weighted vote of the gene, g ; a_g is the correlation between gene expression values and class distinction; $b_g = (\mu_1(g) + \mu_2(g))/2$, which is the average of the mean \log_{10} expression value in a first class and a second class; x_g is the \log_{10} gene expression value in the sample to be tested; and wherein a

positive V value indicates a vote for the first class, and a negative V value indicates a vote for the second class.

13. The method according to Claim 11, wherein the informative genes are selected from the group consisting of the genes in Figure 1.
- 5 14. The method according to Claim 11, wherein the informative genes are selected from the group consisting of the genes in Figures 2A and 2B.
15. A method of classifying a sample according to lymphoma type comprising the steps of:
 - 10 a) isolating a gene expression product from at least one informative gene from one or more cells in said sample; and
 - b) determining a gene expression profile of at least one informative gene, wherein the gene expression profile is correlated with a lymphoma type, thereby classifying the sample with respect to lymphoma type.
- 15 16. A method according to Claim 15, wherein the lymphoma type is diffuse large cell lymphoma.
17. A method according to Claim 15, wherein the lymphoma type is follicular lymphoma.
18. A method according to Claim 15, wherein the gene expression product is mRNA.
- 20 19. A method according to Claim 18, wherein the gene expression profile is determined using hybridization probes specific to one ore more informative genes.

20. A method according to Claim 18, wherein the gene expression profile is determined using oligonucleotide microarrays.
21. A method according to Claim 15, wherein the gene expression product is a peptide.
- 5 22. A method according to Claim 21, wherein the gene expression profile is determined using antibodies.
23. A method according to Claim 15, wherein the informative gene is selected from the group consisting of the genes in Figures 3A and 3B.
24. A method according to Claim 15, wherein the informative gene is selected from the group consisting of the genes in Figures 4A and 4B.
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25. A method of assigning a sample to a lymphoma class, comprising the steps of:
- a) determining a weighted vote for one of the classes of one or more informative genes in said sample in accordance with a model built with a weighted voting scheme, wherein the magnitude of each vote depends on the expression level of the gene in said sample and on the degree of correlation of the gene's expression with class distinction; and
- 15 b) summing the votes to determine the winning class, wherein the winning class is the lymphoma class to which the lymphoma sample is assigned.
- 20 26. The method of Claim 25, wherein the weighted voting scheme is:

$$V_g = a_g (x_g - b_g),$$

wherein V_g is the weighted vote of the gene, g ; a_g is the correlation between gene expression values and class distinction; $b_g = (\mu_1(g) + \mu_2(g))/2$, which is the average of the mean \log_{10} expression value in a first class and a second class; x_g is the \log_{10} gene expression value in the sample to be tested; and wherein a positive V value indicates a vote for the first class, and a negative V value indicates a vote for the second class.

27. The method according to Claim 25, wherein the informative genes are selected from the group consisting of the genes in Figures 3A and 3B.
28. The method according to Claim 25, wherein the informative genes are selected from the group consisting of the genes in Figures 4A and 4B.
29. An oligonucleotide microarray immobilized on a solid support chip, comprising a plurality of oligonucleotide probes specific for one or more informative genes selected from the group consisting of the genes in Figures 1, 2A, 2B, 3A, 3B, 4A and 4B.
30. A method of assessing treatment efficacy in an individual having a lymphoma comprising determining the expression level of one or more informative genes at multiple time points during treatment.
31. The method of Claim 30, wherein a decrease in expression of the one or more informative genes shown to be expressed, or expressed at increased levels as compared with a control, in individuals having a lymphoma or at risk for developing a lymphoma, is indicative that treatment is effective.
32. The method of Claim 31, wherein the lymphoma is a diffuse large cell lymphoma.

33. The method of Claim 31, wherein the one or more informative genes are selected from the group consisting of the genes in Figures 1, 2A, 2B, 3A, 3B, 4A and 4B.
34. The method of Claim 30, wherein an increase in expression of the one or more informative genes shown not to be expressed, or expressed at reduced levels as compared with a control, in individuals having a lymphoma or at risk for developing a lymphoma, is indicative that treatment is effective.
35. The method of Claim 34, wherein the lymphoma is a diffuse large cell lymphoma.
36. The method of Claim 34, wherein the one or more informative genes are selected from the group consisting of the genes in Figures 1, 2A, 2B, 3A, 3B, 4A and 4B.

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